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ABSTRACT

Background The COVID-19 pandemic led to changes in patterns of presentation to emergency departments. Child health professionals were concerned that this could contribute to the delayed diagnosis of life-threatening conditions, including childhood cancer (CC) and type 1 diabetes (T1DM). Our multicentre, UK-based service evaluation assessed diagnostic intervals and disease severity for these conditions.

Methods We collected presentation route, timing and disease severity for children with newly diagnosed CC in three principal treatment centres and T1DM in four centres between 1 January and 31 July 2020 and the corresponding period in 2019. Total diagnostic interval (TDI), patient interval (PI), system interval (SI) and disease severity across different time periods were compared.

Results For CCs and T1DM, the route to diagnosis and severity of illness at presentation were unchanged across all time periods. Diagnostic intervals for CCs during lockdown were comparable to that in 2019 (TDI 4.6, PI 1.1 and SI 2.1 weeks), except for an increased PI in January–March 2020 (median 2.7 weeks). Diagnostic intervals for T1DM during lockdown were similar to that in 2019 (TDI 16 vs 15 and PI 14 vs 14 days), except for an increased PI in January–March 2020 (median 21 days).

Conclusions There is no evidence of diagnostic delay or increased illness severity for CC or T1DM, during the first phase of the pandemic across the participating centres. This provides reassuring data for children and families with these life-changing conditions.

What is known about the subject?

- The UK public health response to the COVID-19 pandemic led to significant changes in emergency department attendances and urgent 2-week wait adult cancer referrals.
- Changes in the number of newly diagnosed type 1 diabetes (T1DM) cases and higher proportions of severe diabetic ketoacidosis (DKA) were also reported, following lockdown in the UK and other countries.
- Child health professionals were concerned that the pandemic could be associated with delayed presentation of children with significant illnesses.

What this study adds?

- The route to diagnosis and severe DKA rate for T1DM showed variability in the early lockdown period.
- Diagnostic intervals for both childhood cancer and T1DM during the first UK national lockdown were comparable to that in 2019, except for increased patient intervals in January–March 2020.

INTRODUCTION

The UK instigated a national lockdown on 23 March 2020 in response to the evolving COVID-19 pandemic. There was an order to stay at home with permission to leave for essential purposes only. These rules were in place in England until the 1 June 2020 and Scotland until the 29 May 2020, when people were permitted to meet outside with up to six and eight people, respectively.[1] However, in general, the lockdown restrictions in the early stages of the pandemic in the UK were very similar across all countries. Specific individuals with conditions that put them at high risk of serious illness from COVID-19 were instructed to 'shield' by remaining at home and avoiding all face-to-face contact.[2]

The UK public health response to the COVID-19 pandemic led to major changes in service utilisation of emergency departments (ED), with an observed 49% reduction in attendances in the week following the March 2020 announcement of lockdown.[3] More specifically, this reduction was also seen in children's ED attendances in both Scotland and Italy.[4 5] This raised concern among

child health professionals that the pandemic could be associated with delayed presentation of children with significant illnesses[6] including life-changing childhood conditions such as type 1 diabetes (T1DM) and childhood cancer (CC). We were concerned there may have been an increase in delays in seeking medical advice (the patient interval (PI)) and/or accessing initial investigations and interventions (the system interval (SI)), leading to a prolongation of the total diagnostic interval (TDI).[7]

In the UK, 1900 children are diagnosed with cancer each year.[8 9] The diverse and often insidious nature of presenting symptoms combined with the low incidence and lack of awareness of childhood malignancy may contribute to a prolongation of the TDI. Recent adult studies[10 11] report that referrals via the urgent 2-week wait pathway for suspected cancer diagnoses decreased by 84% from March to May 2020[11] and 60% in June 2020.[10] One study predicted a reduction of over 10% in 10-year survival of adults with cancer,[11] while another predicted an excess of 1307 cancer deaths.[10] The evidence is equivocal as to whether delays in time to diagnosis is associated with survival from CCs,[11–13] however the psychological and economic distress on families awaiting a CC diagnosis should not be underestimated.[12]

Experience of the COVID-19 pandemic for children with T1DM has been inconsistent. A survey of 53 Italian paediatric diabetes centres found that the number of children with a new diagnosis of diabetes from February to April 2020 was 23% lower than the corresponding period in 2019. The survey also found the proportion of patients presenting with severe diabetic ketoacidosis (DKA) was increased.[14] A 30-patient UK study reported an apparent increase in new-onset T1DM during the first 6 weeks of lockdown.[15]

The aim of the project was to assess any association of the COVID-19 pandemic on new diagnoses of CC and T1DM at participating UK centres.

METHODS

Study design

We undertook a multicentre service evaluation using existing clinical case data assessing the route of diagnosis, diagnostic interval and severity of presentation.

Eligibility criteria were:

1. All children who attended three centres (the Royal Hospital for Sick Children (RHSC), Edinburgh, Leeds Teaching Hospitals NHS Trust and Nottingham University Hospitals (NUH) NHS Trust) and were diagnosed with cancer between 1 January and 30 June 2019 and the corresponding period in 2020.
2. All children who attended four centres (the RHSC, Edinburgh, NUH NHS Trust, University Hospital Wishaw and Ninewells Hospital, Dundee) and were diagnosed with T1DM between 1 January and 31 July 2019 and the corresponding period in 2020.

All centres were the central referral centres for children within their region who received a new diagnosis of cancer or of T1DM.

A standard proforma (online supplemental files 1 and 2) was used to retrospectively collect information on demographics, diagnosis, referral pathway and clinical presentation. We also collected information on whether patients were shielding at presentation (following specific government guidelines to minimise risk of SARS-CoV-2 exposure for those considered clinically extremely vulnerable). Dates of symptom onset, first presentation to healthcare and final diagnosis were used to calculate TDI (time between symptom onset to diagnosis), PI (time between symptom onset to first presentation) and SI (time between first presentation to diagnosis).[7] Data were collected and entered into a centralised database by named individuals at the participating centres. Data were double checked at the point of entry to the database and then reviewed by the database administrator. Any discrepancies or queries from the database administrator were then highlighted and re-reviewed by the data collectors at each centre.

Statistical analysis

Descriptive analyses, χ^2 test and Mann-Whitney U or Kruskal-Wallis tests were used to describe patterns of referral and illness, comparing the differences of key measures among different time periods (1 January–31 March 2020 and 1 April–31 July 2020 and the corresponding period in 2019). Pairwise comparisons of proportions were carried out using the Z test with Bonferroni corrections. All analyses were performed with IBM SPSS V.26.0 for Windows (IBM Corp. Armonk, New York, USA) and $p<0.05$ was considered statistically significant.

RESULTS

Study population

Childhood cancer

There were 253 new diagnoses of CC during the study period (table 1). Of these, 164 (64%) were male and 55 (22%) were from a black, Asian and minority ethnic (BAME) background. Patients were diagnosed at one of three principal treatment centres (Edinburgh=64, Leeds=100, Nottingham=89). There were no significant differences in the distribution of gender, ethnic background or age at diagnosis between study periods (table 1). The proportion of tumour type in each evaluation period did not change. Overall, 95% (53/56) of patients who presented during the lockdown period were not shielding.

Overall, there was a 17% reduction in number of incident CC cases between 2019 (n=138) and 2020 (n=115). This change varied between centres (4% increase to 40% reduction) (figure 1).

Type 1 diabetes

There were 187 new diagnoses of T1DM during the study period (table 2). Of these, 90 (48%) were male and 18 (10%) were from a BAME background. Patients were diagnosed at one of the four participating centres (Edinburgh=45,

Table 1 Summary of incident childhood cancer patient characteristics (n=253)

	Total (n=253)		January–June 2019 (n=138)		January–March 2020 (n=59)		April–June 2020 (n=56)		
	n	Col%	n	Col%	n	Col%	n	Col%	value
Gender									0.150
Male	162	64%	81	59%	41	69%	40	71%	
Female	91	36%	57	41%	18	31%	16	29%	
Age (years)									0.963
Under 5	99	39%	53	38%	25	43%	21	38%	
5–11	92	37%	52	38%	19	33%	21	38%	
12+	61	24%	33	24%	14	24%	14	25%	
BAME background									0.945
No	198	78%	107	78%	47	80%	44	79%	
Yes	55	22%	31	22%	12	20%	12	21%	
COVID-19 isolation/shielding									
No	250	99%	138	100%	59	100%	53	95%	
Yes	3	1%	0	0%	0	0%	3	5%	
Tumour type									0.273
Leukaemia	69	27%	33	24%	17	29%	19	34%	
CNS tumour	74	29%	48	35%	14	24%	12	21%	
All other tumour types	110	43%	57	41%	28	47%	25	45%	
ICU stay									0.275
No	223	88%	120	87%	55	93%	48	86%	
Yes	26	10%	17	12%	3	5%	6	11%	
Not known	4	2%	1	1%	1	2%	2	4%	
HCP visits before diagnosis									0.569
3 or less	152	60%	82	59%	40	68%	30	54%	
4–6	64	25%	38	28%	12	20%	14	25%	
7–9	21	8%	11	8%	3	5%	7	13%	
10 or more	16	6%	7	5%	4	7%	5	9%	

BAME, black, Asian and minority ethnic; CNS, Central Nervous System; Col%, Column Percentage; HCP, Healthcare Professionals; ICU, Intensive Care Unit.

Dundee=30, Wishaw=53, Nottingham=59). There were no significant differences in gender, ethnic background or age at diagnosis between the study periods (table 2). Overall, 91% (42/46) of those who presented during the lockdown period were not shielding.

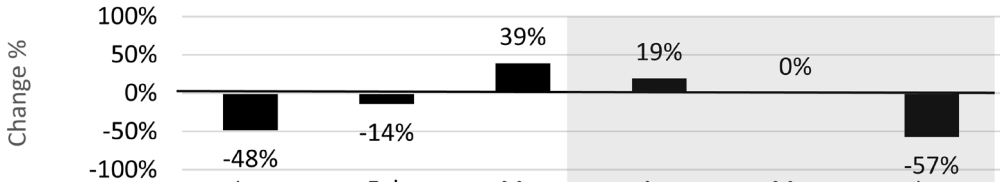
A reduction in the numbers of new cases of T1DM between the months of April and July 2020 and the identical period in 2019 occurred in three of the four units. Overall, there was a 3%–24% reduction in new diagnoses of T1DM between the months of January and July 2020 compared with the corresponding period in 2019 in all centres (figure 1).

Route to diagnosis

Childhood cancer

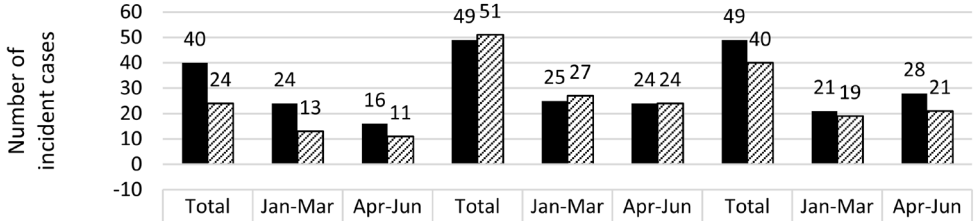
Across all time points, 60% of children (152/253) were diagnosed within three or fewer healthcare contacts, 25% within four to six contacts, 8% within seven to nine contacts and 6% required more than 10 contacts prior to diagnosis. There was no significant difference in distribution across three time periods (p=0.569) or January–March 2020 and April–June 2020 (p=0.359) (online supplemental figure S1a). General practice was the first point of healthcare contact in about half of the patients across all time periods (54% in 2019, 49% in January–March 2020, 48% in April–June 2020) (online supplemental figure S1b). Overall, 63% of patients presented to hospital as an emergency presentation either from primary care or to the ED. Overall, 36% of children had their diagnostic investigation requested as an inpatient. These proportions were consistent across all three time periods (p=0.405) (online supplemental figure S1c).

(A) Childhood cancer



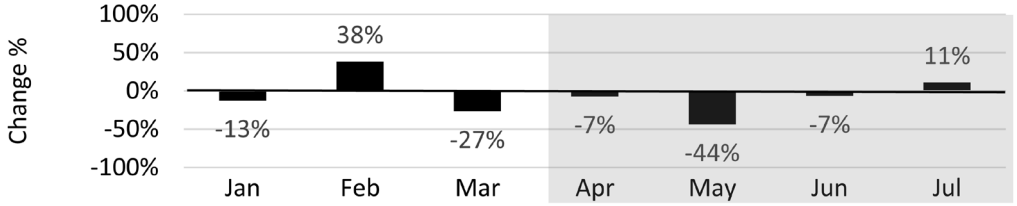
	Jan	Feb	Mar	Apr	May	Jun
2019	31	21	18	21	19	28
2020	16	18	25	25	19	12
Change %	-48%	-14%	39%	19%	0%	-57%

(B) Childhood cancer



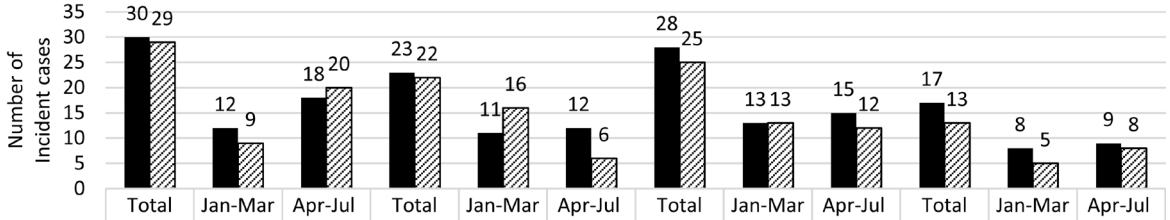
	Total	Jan-Mar	Apr-Jun	Total	Jan-Mar	Apr-Jun	Total	Jan-Mar	Apr-Jun
	Edinburgh			Leeds			Nottingham		
2019 (n=138)	40	24	16	49	25	24	49	21	28
2020 (n=115)	24	13	11	51	27	24	40	19	21
Change %	-40%	-46%	-31%	4%	8%	0%	-18%	-10%	-25%

(C) T1DM



	Jan	Feb	Mar	Apr	May	Jun	Jul
2019 (n=98)	16	13	15	14	16	15	9
2020 (n=89)	14	18	11	13	9	14	10
Change %	-13%	38%	-27%	-7%	-44%	-7%	11%

(D) T1DM



	Total	Jan-Mar	Apr-Jul	Total	Jan-Mar	Apr-Jul	Total	Jan-Mar	Apr-Jul	Total	Jan-Mar	Apr-Jul
	Nottingham			Edinburgh			Wishaw			Dundee		
2019 (n=98)	30	12	18	23	11	12	28	13	15	17	8	9
2020 (n=89)	29	9	20	22	16	6	25	13	12	13	5	8
Change %	-3%	-25%	11%	-4%	45%	-50%	-11%	0%	-20%	-24%	-38%	-11%

Figure 1 Number of newly diagnosed of childhood cancer and type 1 diabetes (T1DM) cases between January and July 2020 compared with the corresponding period in 2019. (A, C) Data covers all participating centres contributing data to the project by month. Shaded areas indicate national lockdown months. (B, D) Data by individual centre over the periods January–June/July in 2019 and 2020.

Table 2 Summary of incident T1DM patient characteristics (n=187)

	Total (n=187)		January–July 2019 (n=98)		January–March 2020 (n=43)		April–July 2020 (n=46)		
	n	Col%	n	Col%	n	Col%	n	Col%	p value
Gender									0.718
Male	90	48%	46	47%	23	53%	21	46%	
Female	97	52%	52	53%	20	47%	25	54%	
Age (years)									0.174
Under 5	32	17%	22	22%	5	12%	5	11%	
5–11	87	47%	43	44%	18	42%	26	57%	
12+	68	36%	33	34%	20	47%	15	33%	
BAME background									0.484
No	168	90%	87	89%	41	95%	40	89%	
Yes	18	10%	11	11%	2	5%	5	11%	
COVID-19 isolation/shielding									0.012
No	183	98%	98	100%	43	100%	42	91%	
Yes—self-isolation	3	2%	0	0%	0	0%	3	7%	
Yes—shielding	1	1%	0	0%	0	0%	1	2%	
Diabetic ketoacidosis									0.624
No	112	60%	59	61%	26	60%	27	59%	
Mild/Moderate	46	25%	25	26%	12	28%	9	20%	
Severe	28	15%	13	13%	5	12%	10	22%	
Ventilation									0.607
No	182	97%	94	96%	43	100%	45	98%	
Yes	5	3%	4	4%	0	0%	1	2%	
ICU stay									0.625
No	169	91%	90	92%	39	93%	40	87%	
Yes	17	9%	8	8%	3	7%	6	13%	
HCP visits before diagnosis									0.673
1	164	92%	87	92%	37	95%	40	89%	
>1	15	8%	8	8%	2	5%	5	11%	

BAME, black, Asian and minority ethnic; Col%, Column Percentage; HCP, Healthcare Professionals; ICU, Intensive Care Unit; T1DM, type 1 diabetes.

Type 1 diabetes

The source of referral leading to diagnosis was the ED in 30% (14/46) of cases between April and July 2020. This compared with 12% (5/43) of cases diagnosed between January and March 2020 (p=0.091) and 19% (19/98) of cases diagnosed over the period of January–July 2019 (p=0.426). Overall, 63% of patients had been referred by their General Practitioner (GP) between April and July 2020, compared with 81% of patients in the preceding 3 months, and 72% of patients in 2019 (online supplemental figure S2).

Time to diagnosis

Childhood cancer

Across all three centres, there was no significant difference in the distribution of TDI between 2019 (median 4.5, IQR 2.3–10.9 weeks) and January–March 2020 (median 5.6, IQR 3.4–15.3 weeks) or April–June 2020 (median 4.6, IQR 2.7–11.9 weeks) (p=0.351) (figure 2 and online supplemental figure S3a). There was a significant increase in PI between 2019 and January–March 2020 (median 0.9, IQR 0.1–2.1 vs median 2.7, IQR 0.7–4.4 weeks, p=0.005), but during April–June 2020 there was no significant difference compared with 2019 (median 1.1, IQR 0.3–4.7 vs median 0.9, IQR 0.1–2.1 weeks, p=0.383) (figure 2). SI was stable across all time points (figure 2). The pattern remained the same when the 2019 data were further split into January–March and April–June (online supplemental figure S5). Differences in PI across four time periods was significant (p=0.011) and pairwise comparisons showed that PI in January–March 2020 was significantly higher than that in the January–March 2019 (median 2.7, IQR 0.7–4.4 vs median 0.6, IQR 2.0 weeks, p=0.008).

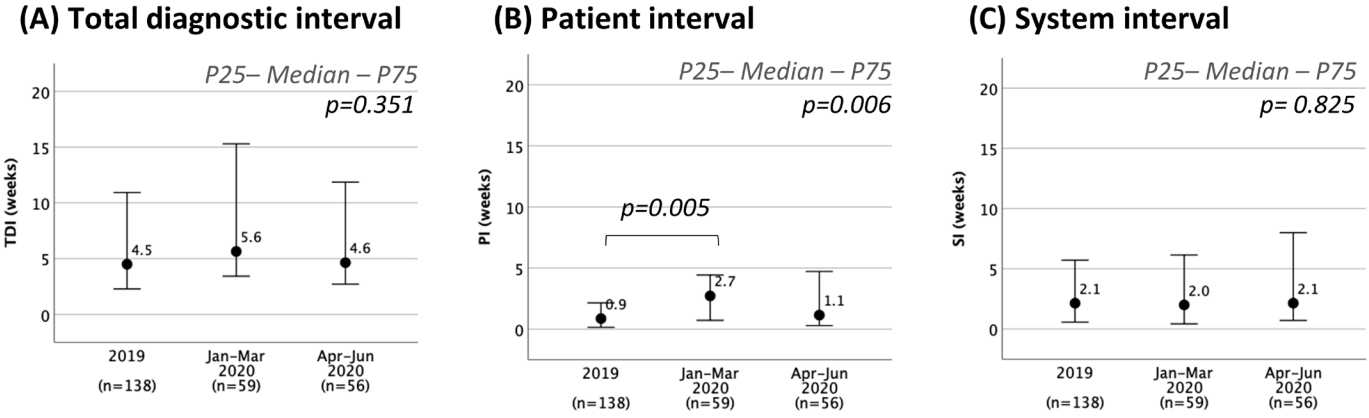


Figure 2 Time to diagnosis for childhood cancer. (A) Total diagnostic interval (TDI): interval between first symptom onset to diagnosis. (B) Patient interval (PI): time from initial symptom onset to first presentation to healthcare. (C) System interval (SI): time between first presentation to healthcare to diagnosis.

There was no significant difference in TDI across all time periods for leukaemias, CNS tumours and solid tumours in subgroup analyses (figure 3). There was no significant difference in PI or SI for individual principal treatment centres or tumour types (figure 3 and online supplemental figure S3b,c).

Type 1 diabetes

Median TDIs for incident T1DM cases were 16 (IQR 8–28), 21 (IQR 14–32) and 15 (7–22) days for 2019, January–March 2020 and April–July 2020, respectively. There was no significant difference across the three time periods (p=0.119). A similar pattern was observed in PI. The comparison across all time periods was not significant (p=0.054), subanalyses showed that PI was longer during January–March 2020 compared with April–July 2020 (median 21, IQR 14–32 vs median 14, IQR 7–22 days, p=0.025) and 2019 (median 14, IQR 7–28 days, p=0.036) (figure 4 and online supplemental figure S4).

When the 2019 data were further split into January–March and April–June, differences in PI across four time periods became significant (p=0.041) and none of the post hoc pairwise comparisons reached significant level (online supplemental figure S6).

Severity of presentation

Childhood cancer

Within 7 days of diagnosis, 10% (26/253) of patients with CC required admission to paediatric intensive care. This was stable across all time periods (p=0.275) (table 1).

Type 1 diabetes

The proportion of patients presenting in DKA was 41% (19/46) in the period April–July 2020, 40% (17/43) for the time period January–March 2020 and 39% (38/98) for the time between January and July 2019. There was no significant difference in the proportion of patients in DKA across all time periods. The proportion of children presenting with severe DKA (pH <7.1, serum bicarbonate <5 mmol/L)[16] showed no statistical difference between lockdown April–July 2020 (22%, 10/46) compared with 12% (5/43) January–March 2020 and 13% (13/98) January–July 2019) in the periods prior to lockdown (p=0.447). There was no significant difference in the rate of intensive care admission or requirement for ventilatory support (table 2).

DISCUSSION

We have demonstrated that the first phase of the COVID-19 pandemic was not associated with route of presentation, TDI or disease severity at presentation for children with a new diagnosis of CC or T1DM at the study centres. Given the reported reduction in paediatric ED attendance,[17 18] it had been predicted that both the PI and TDI would be prolonged and clinical presentations would be more severe. This prediction was not supported by our study.

A snapshot survey was commissioned in April 2020 by the Child Cancer Smart Team in conjunction with the Childhood Cancer and Leukaemia Group (CCLG) to obtain the absolute numbers of new diagnoses of CC at each principal treatment centre in the UK (online supplemental file 3). This survey revealed 27% fewer new cases in April 2020 compared with April 2019, raising concerns about the potential for diagnostic delay. Similar anxieties had been expressed related to delayed presentation of patients with T1DM.[19] One survey of diabetes units in the UK reported that 20% of children and young people diagnosed with T1DM between 1 March and 30 June 2020 had had a delayed presentation. Reasons for this included fear of contracting SARS-CoV-2 as well as limited access to GP services.[15]

Similarities between type 1 diabetes and childhood cancer presentations

While T1DM and CC cancer are different in terms of their presentations, we chose to investigate them together because they are both relatively rare, yet well recognised and potentially life-threatening conditions. We found no evidence that either of these conditions were associated

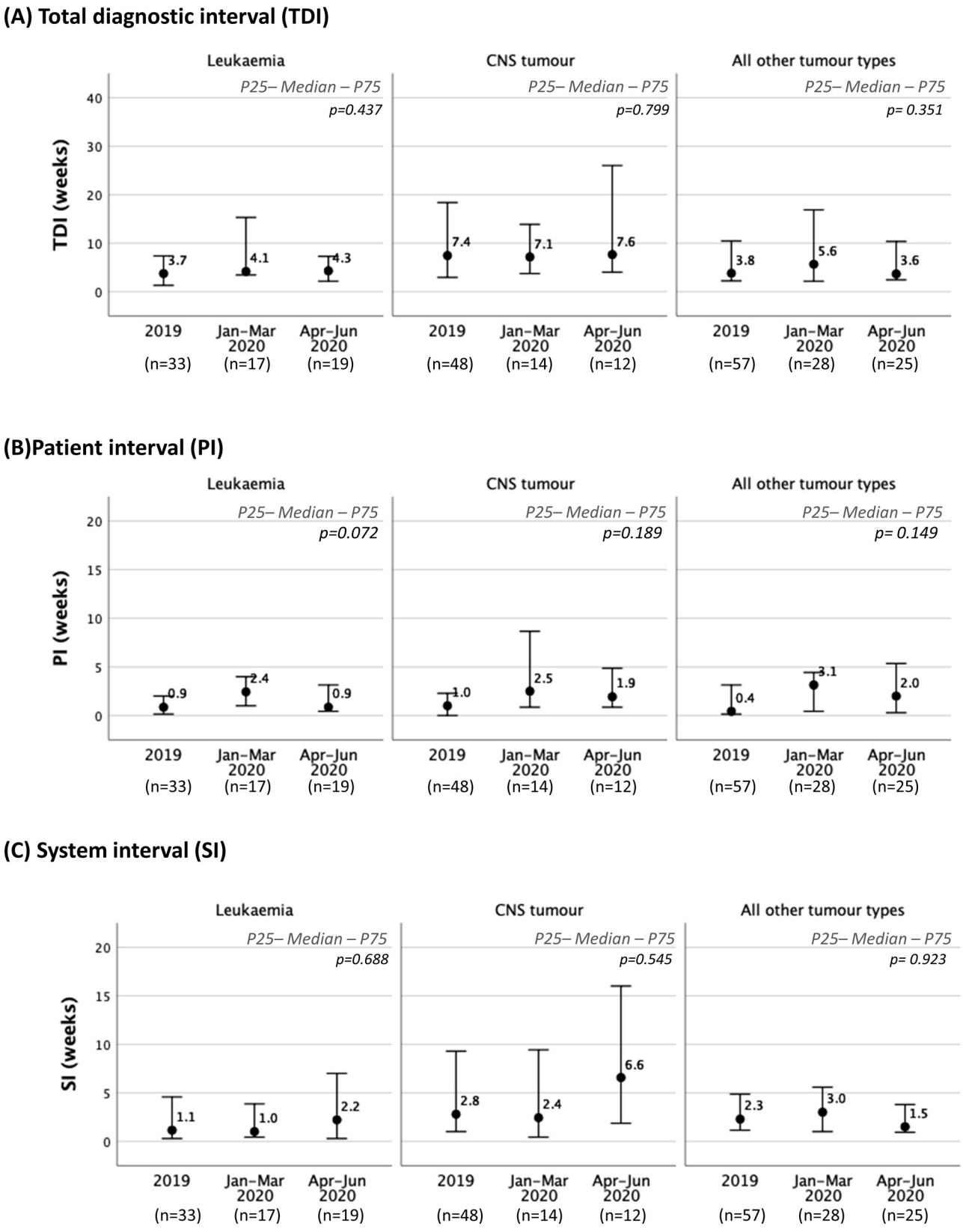


Figure 3 Time to diagnosis for childhood cancer for leukaemia, CNS (Central Nervous System) tumour and all other tumour types combined. (A) Total diagnostic interval (TDI): interval between first symptom onset to diagnosis. (B) Patient interval (PI): time from initial symptom onset to first presentation to healthcare. (C) System interval (SI): time between first presentation to healthcare to diagnosis.

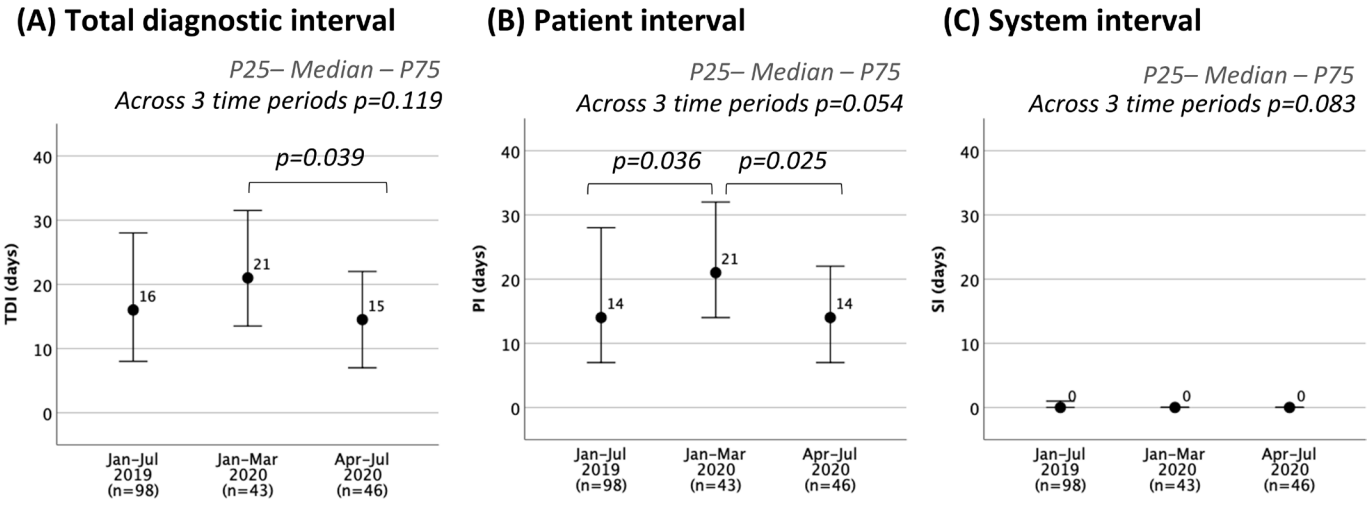


Figure 4 Time to diagnosis of incident T1DM cases between January and July 2020 and corresponding period in 2019. (A) Total diagnostic interval (TDI): interval between first symptom onset to diagnosis. (B) Patient interval (PI): time from initial symptom onset to first presentation to healthcare. (C) System interval (SI): time between first presentation to healthcare and diagnosis.

with delayed presentations associated with the pandemic. Other similarities include a higher PI during January–March 2020 and a shift from presentation via the general practitioner to the emergency department.

We demonstrated higher PI during January–March 2020 for patients with CC and T1DM. This may reflect a period of uncertainty for patients and healthcare systems in preparation for the first phase of the pandemic. There was widespread UK media coverage of the approaching pandemic and we hypothesise that this may have resulted in families initially avoiding healthcare services. Further work will be required to establish whether this hypothesis can be substantiated with evidence from the behaviour and beliefs of service users themselves. The subsequent reduction in PI during and after lockdown suggests no significant delay in caregivers seeking medical attention for children, which may reflect increased public health messaging that was not initially present during the lead up to lockdown and the pandemic.

While there was variability between units, there was evidence of a shift towards first presentations to ED from primary care, for patients with CC and T1DM. While we did not identify statistically significant changes, we recommend that each treatment centre evaluate any change in how their services have been accessed during the pandemic, to assist in future service planning.

Type 1 diabetes

A study of the North-West London Paediatric Diabetes Network between 23 March and 4 June 2020 reported an apparent increase in cases of new-onset T1DM in two of the five units.[15] Overall, 21/30 children with a new diagnosis presented with DKA, 52% of which were severe. These are generally considered to represent high rates of both of DKA and severe DKA in newly diagnosed patients. However, the number of children involved in this study was small, no comparisons were possible with other time periods and we were unable to replicate the findings.

In a large survey of 53 Italian paediatric diabetes centres, the number of newly diagnosed children with T1DM and DKA were similar to 2019.[14] However, the proportion of all patients with T1DM who developed severe DKA was significantly greater in 2020 (44.3% vs 36.1%, p=0.03).[14] Despite not being significant, the pattern of our results are similar to the Italian experience[14] which demonstrated a 9% reduction in new diagnoses of T1DM when comparing January–July 2020 to January–July 2019. Our data showed a 7%–44% reduction in 3 of the 4 months following lockdown in new cases of T1DM, with a 27% decrease during March 2020 when national lockdown was announced. The incidence of DKA at presentation was stable between the measured time periods, however the incidence of severe DKA was slightly worse following lockdown (22% (April–July 2020) vs 12% (January–March 2020) vs 13% (January–July 2019)).

The increased incidence of severe DKA among patients diagnosed post lockdown, while not significant, is a concern. This finding is consistent with the Italian data and with other units in the UK.[14 19] It initially appears to be counterintuitive when one takes into account the reduction in the TDI and PI post lockdown. However, it is well recognised that some children with T1DM can present acutely with rapid onset of ketoacidosis. The increased rate of severe DKA at presentation serves to emphasise the importance of the ongoing provision of public health campaigns to raise awareness of the symptoms of T1DM among parents/caregivers.[20]

Childhood cancer

Overall, TDI for CCs was stable between the three time periods. Consistent with previously published evidence,[13] the TDI for leukaemia was shorter than for CNS tumours,

suggesting that the COVID-19 pandemic did not disturb this pattern.

A large cross-sectional survey from the Paediatric Oncology East and Mediterranean Group reported that some centres noticed that all newly diagnosed patients experienced delays in diagnosis during the pandemic.[21] This was thought to be due to: (1) patients refusing to present for essential visits for fear of contracting COVID-19; (2) hospital staff being relocated to other areas and (3) governmental decisions affecting the availability of public transport and freedom of travel. Although in the UK during the first lockdown the availability of public transport was decreased and in some tertiary oncology centres paediatric hospital staff were redeployed, our data does not support a similar situation in the participating centres.

Overall, 10% of new CC diagnoses in this study required intensive care within 7 days of admission, the majority of these had CNS tumours, most likely due to the requirement for early neurosurgery. From this we infer that patients diagnosed during the pandemic were not more unwell than if they had been diagnosed earlier. We recognise that intensive care admission resulting from treatment can occur in the early stages post diagnosis.[22] Consequently, using intensive care admission may overestimate initial disease severity. Reassuringly, a CCLG Study reported that children with cancer and SARS-CoV-2 infection do not appear at increased risk of severe infection compared with the general paediatric population.[23]

Study limitations

Only four UK centres were involved, therefore the study lacked the ability to detect national variations in patterns of presentation. Given the retrospective nature of our study, we cannot exclude the possibility of incomplete areas of data collection, since that some of the children in the service evaluation will have been treated in more than one centre. We believe that this effect is both random and minimal across the centres. Our data collection approaches used a standardised electronic form replicated across all centres. Data were entered by individuals at each centre and double checked by the same individual at the point of entry to the database. Data were subsequently assessed and cleaned by the database administrator and any discrepancies or queries were sent back to the individual who had collected the data for resolution. With more resource we would have used double data entry techniques and the fact that we were unable to do this represents a limitation of our study.

Given the resources available for this service evaluation, we elected to collect comparison data for 1 year prior to the pandemic (2019). However, we recognise that fluctuation occurs and a longer period of prepandemic data collection would have provided greater insight into this variation. It was reassuring however that the incident cases of CC across the UK as a whole remained stable from 2013 to 2017.[24]

In view of the fluid situation of the pandemic, data collection was completed in July 2020 as we believed that timely presentation could inform local practice. We will continue data collection to account for the diagnostic lag for specific diseases including brain tumours. Data collection at a more comprehensive national level would also provide greater clarity on diagnostic intervals. Furthermore, it is important to establish whether subsequent public health measures are associated with longer time to diagnosis due to an evolving backlog of patient referrals across the UK.

CONCLUSIONS

This project was born out of a desire to understand the diagnostic intervals and severity of two life-changing childhood diagnoses during the COVID-19 pandemic. Our findings suggest that public health measures, imposed to control the spread of the pandemic during the first lockdown in the UK, were not associated with delayed diagnosis of CC or T1DM at participating centres. This is good news in the context of a pandemic that has been harmful to children's health and well-being in many other ways. We believe that our study can play a key role in allaying parental and professional concern.

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Contributors J-FL and DS were involved in the designing of study methodology, data collection form and planning the data analysis. RM, MB, KB, RMcL, NTC, TR, MD, PS and GW identified eligible cases. RM, EB, KB, RMcL, NTC, TR, AC, JL and GW collected data at local centres. J-FL conducted the statistical analysis. GW and RMcL wrote the first draft of the manuscript. GW, RMcL, J-FL, TR, MB, RM, MD and PS were involved in editing and reviewing the manuscript. All authors contributed to and have approved the final manuscript. DW supervised the study.

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Competing interests None.

Patient and public involvement statement The data were collected to inform healthcare professionals and the public about presentation route, timing and disease severity for children with newly diagnosed childhood cancer and type 1 diabetes during the COVID-19 pandemic. Due to the unprecedented, urgent need for the data, patients and the public were not involved.

Patient consent for publication Not required.

Ethics approval The protocol was approved by Caldicott guardians of all centres involved.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

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Figure S1 Referral pathway and route to diagnosis of 253 incident childhood cancer cases diagnosed between January and June 2019 and corresponding period in 2020. (a) Number of healthcare professional visits before diagnosis **(b)** First healthcare professional patient/parents approached **(c)** Patient's place of care when the investigation that identified the tumour was requested **(d)** Incidental finding **(e)** Source of referral leading to diagnosis. Emergency presentation is defined as an emergency route via A&E, emergency GP referral, emergency consultant outpatient referral, emergency transfer, emergency admission or attendance. GP referral includes Two Week Wait (urgent GP referrals with a suspicion of cancer), as well as routine and urgent referrals where the patient was not referred under the Two Week Wait referral route.

Figure S2 Referral pathway and route to diagnosis of 187 incident Type 1 diabetes cases diagnosed between January and July 2019 and corresponding period in 2020. (a) Number of healthcare professional visits before diagnosis **(b)** First healthcare professional patient/parents approached **(c)** Patient's place of care when the diagnostic investigation was requested **(d)** Incidental finding **(e)** Source of referral leading to diagnosis. Emergency presentation is defined as an emergency route via A&E, emergency GP referral, emergency consultant outpatient referral, emergency transfer, emergency admission or attendance. GP referral includes routine and urgent referrals.

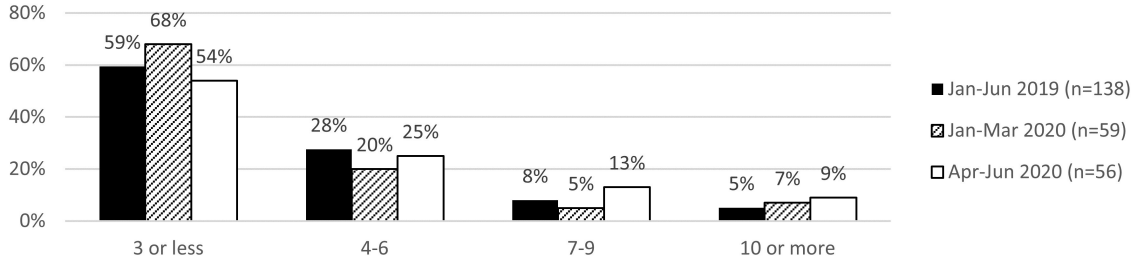
Figure S3. Time to diagnosis in paediatric oncology for each principal treatment centre. **(a)** Total diagnostic interval (TDI): interval between first symptom onset to diagnosis. **(b)** Patient interval (PI): time from initial symptom onset to first presentation to healthcare. **(c)** System interval (SI): time between first presentation to healthcare to diagnosis

Figure S4. Time to diagnosis of incident T1DM cases between January and July 2020 and corresponding period in 2019 by individual centre. (a) Total diagnostic interval (TDI): interval between first symptom onset to diagnosis. **(b)** Patient interval (PI): time from initial symptom onset to first presentation to healthcare.

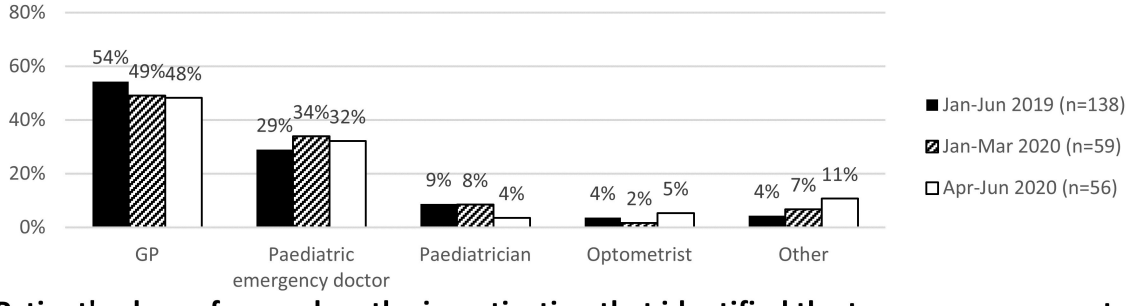
Figure S5 Time to diagnosis for paediatric oncology. **(a)** Total diagnostic interval (TDI): interval between first symptom onset to diagnosis. **(b)** Patient interval (PI): time from initial symptom onset to first presentation to healthcare. **(c)** System interval (SI): time between first presentation to healthcare and diagnosis

Figure S6 Time to diagnosis of incident T1DM cases between January and July 2020 and corresponding period in 2019. (a) Total diagnostic interval (TDI): interval between first symptom onset to diagnosis. **(b)** Patient interval (PI): time from initial symptom onset to first presentation to healthcare. **(c)** System interval (SI): time between first presentation to healthcare to diagnosis

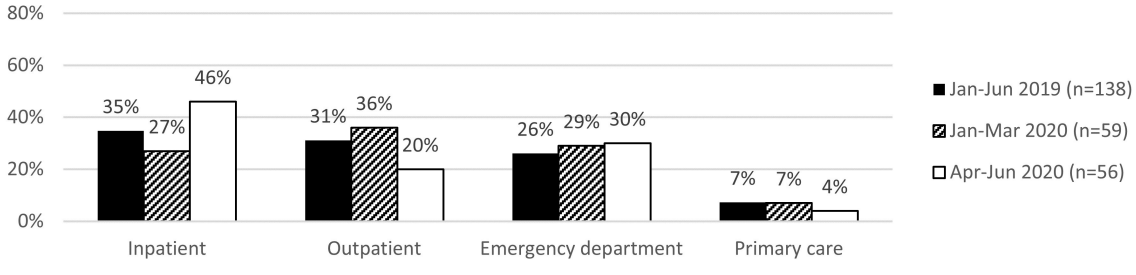
(a) Healthcare professional (HCP) visits before diagnosis



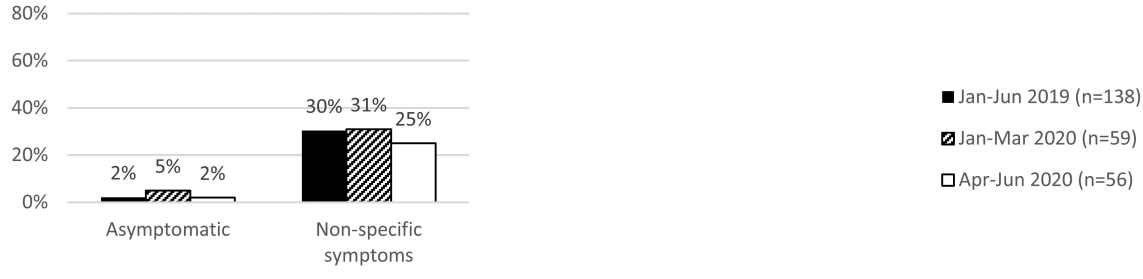
(b) First HCP patient/parent approached



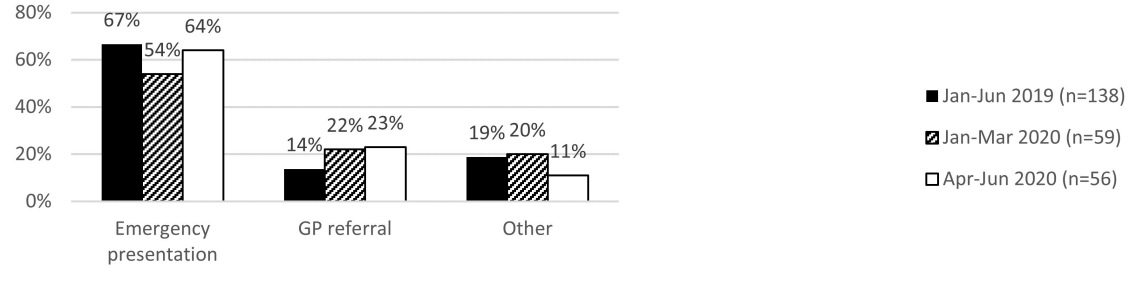
(c) Patient's place of care when the investigation that identified the tumour was requested:



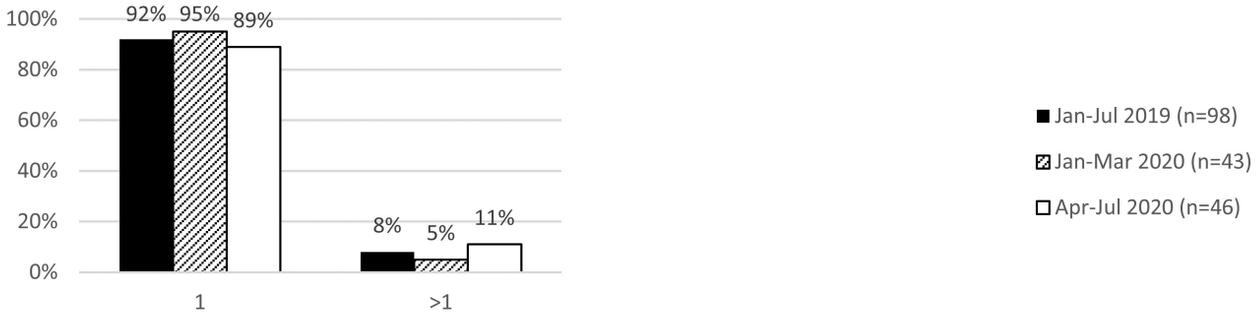
(d) Incidental finding



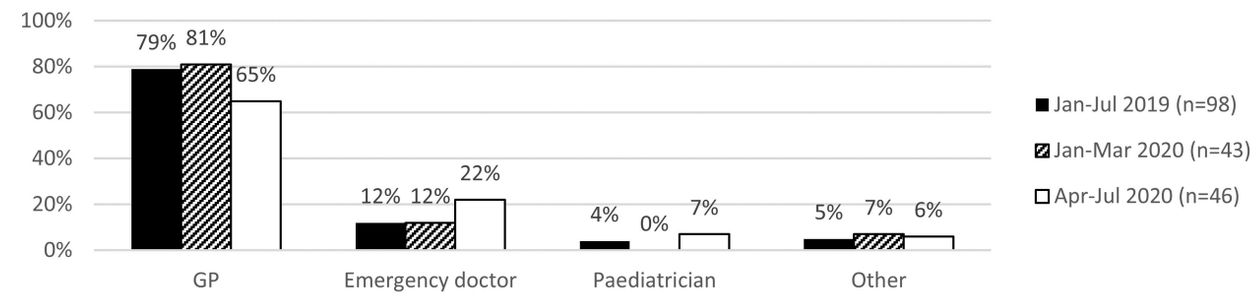
(e) The source of referral leading to diagnosis



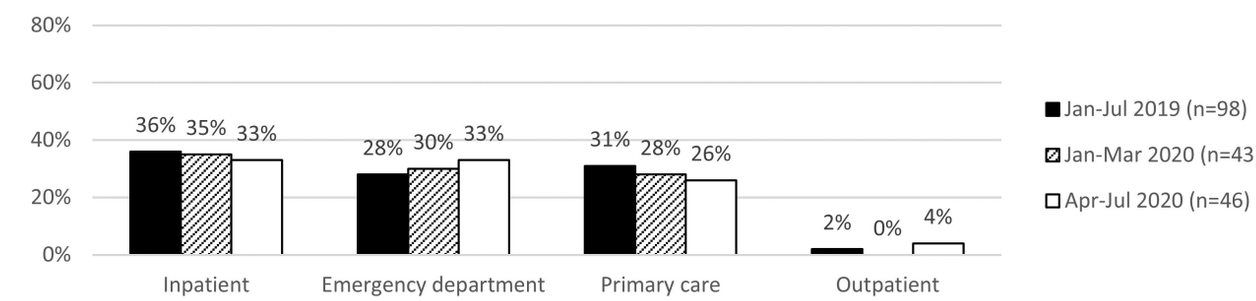
(a) Healthcare professional (HCP) visits before diagnosis



(b) First HCP patient/parent approached

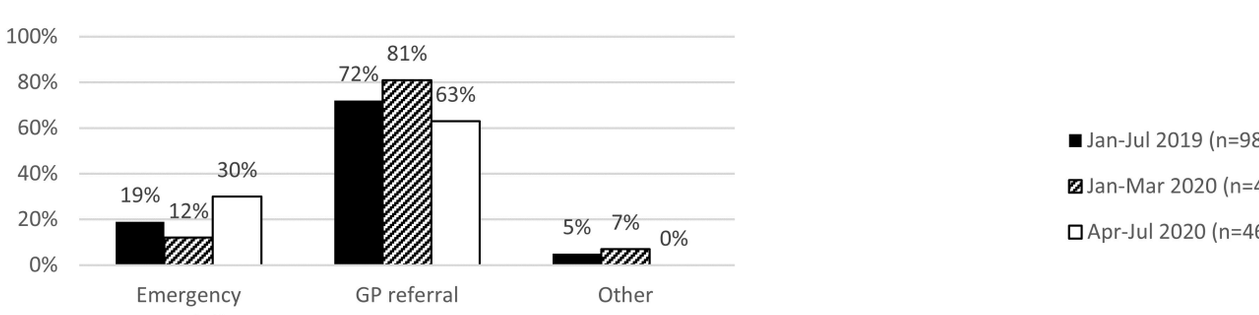


(c) Patient's place of care when the diagnostic investigation was requested:

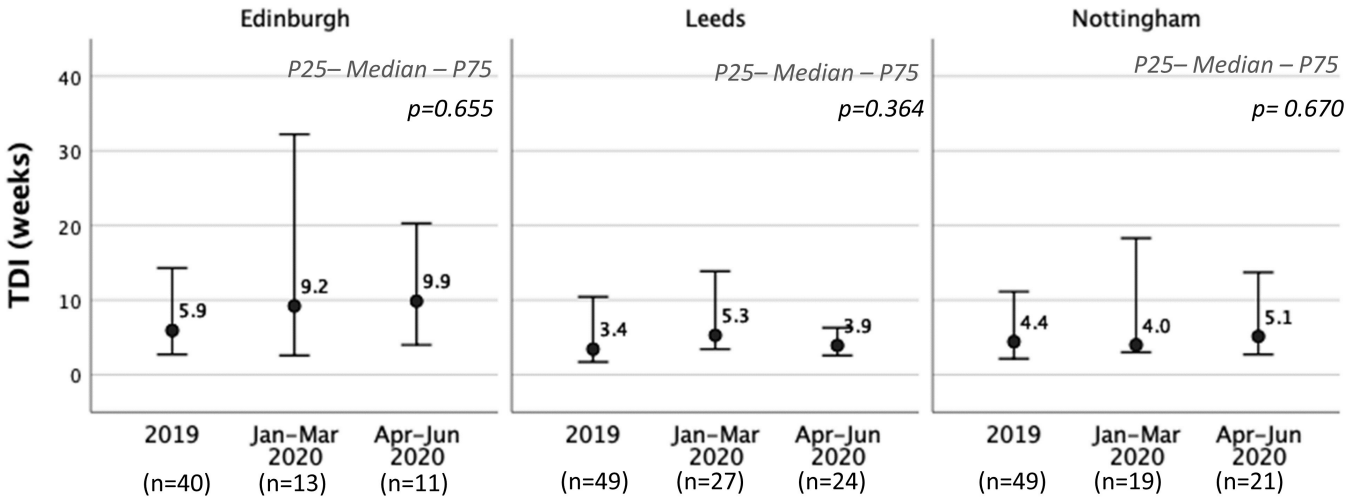


(d) Incidental finding

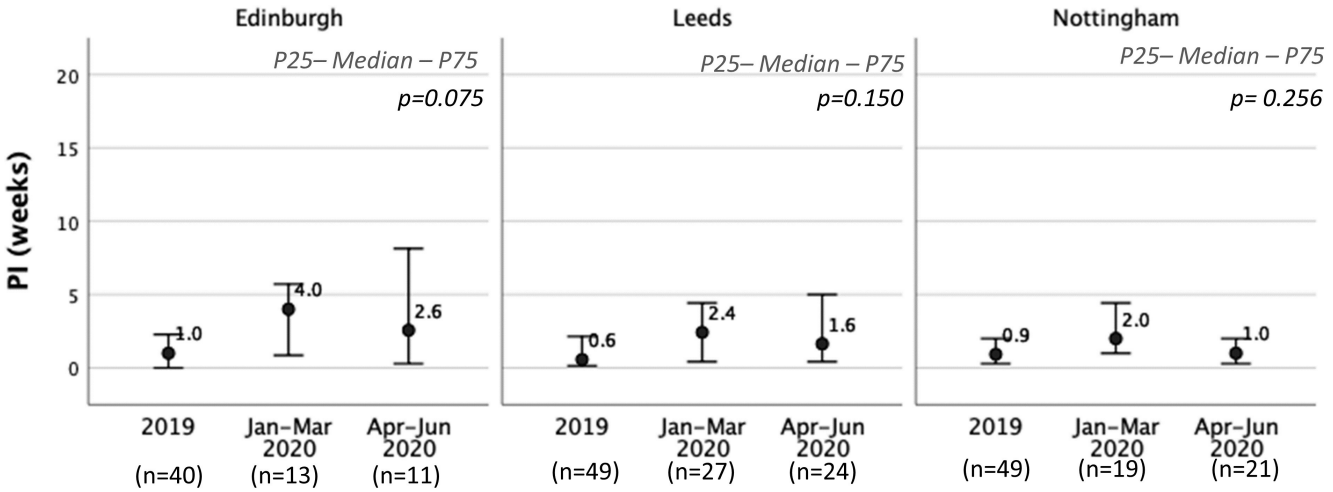
(e) The source of referral leading to diagnosis



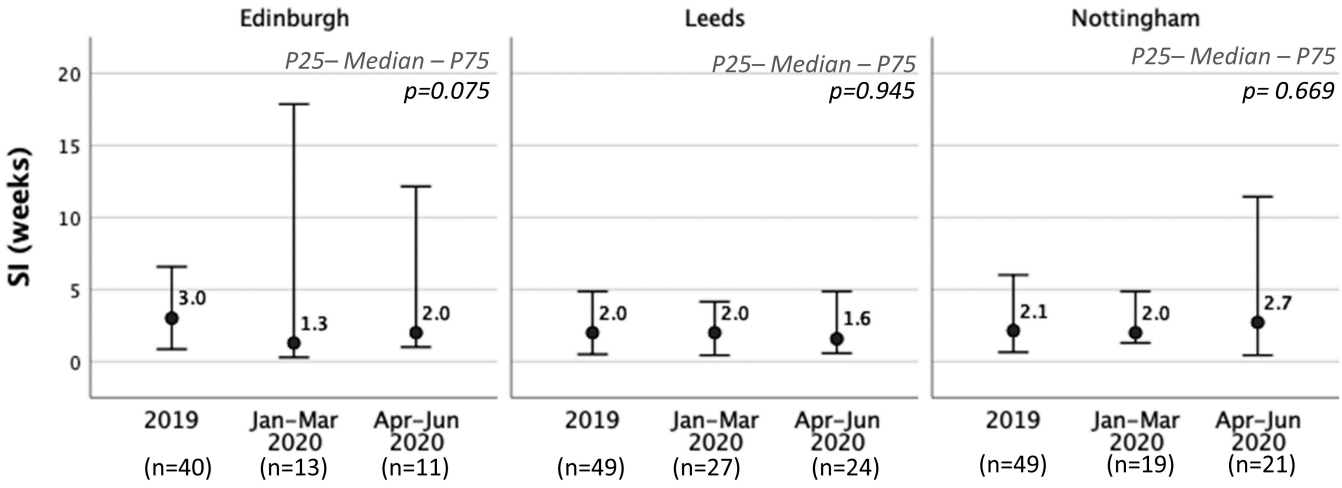
(a) Total diagnostic interval (TDI)



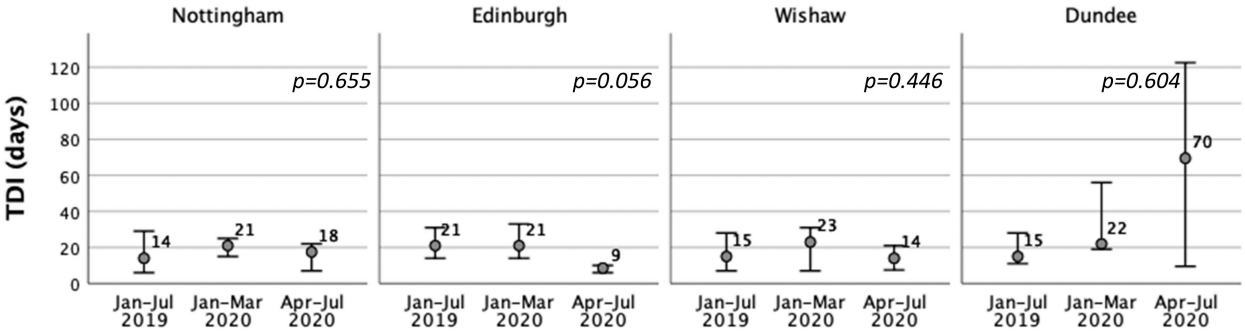
(b)Patient interval (PI)



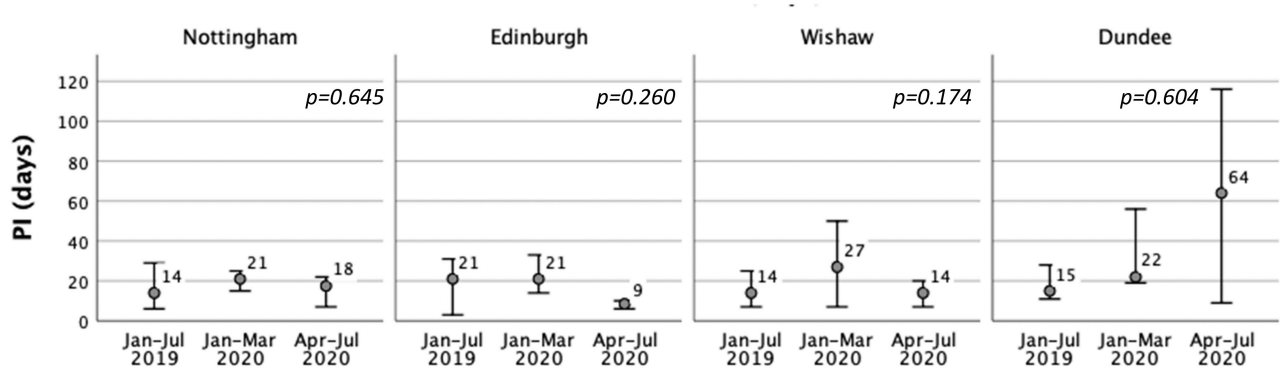
(c) System interval (SI)

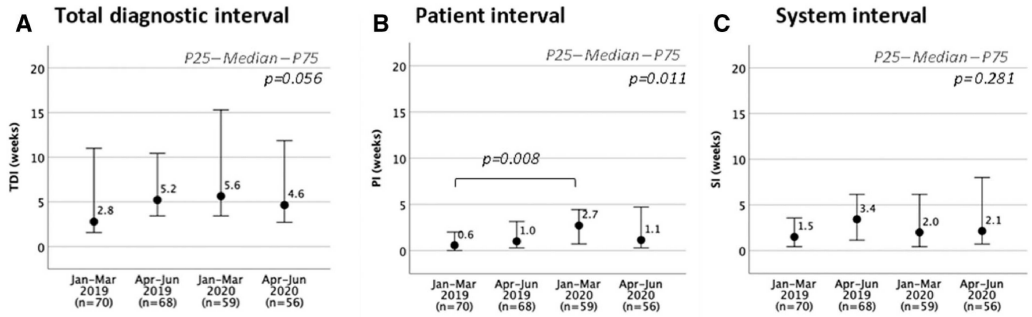


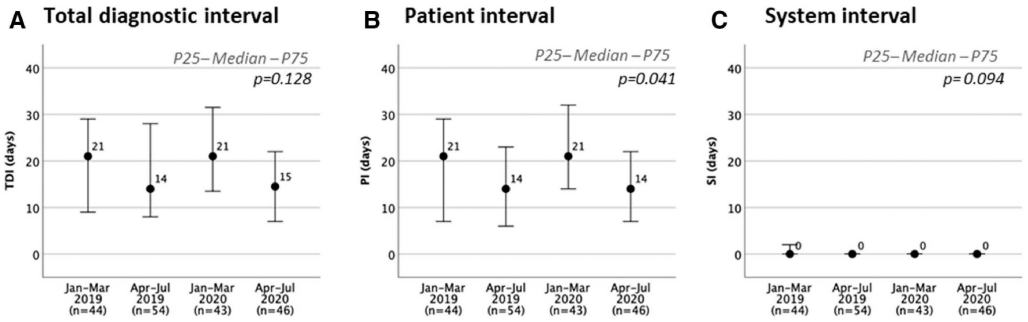
(a) Total diagnostic interval *P25– Median – P75*



(b) Patient interval *P25– Median – P75*




A
Total diagnostic interval
P25–Median–P75
p=0.056
TDI (weeks)
20
15
10
5
0
2.8
5.2
5.6
4.6
Jan–Mar 2019 (n=70)
Apr–Jun 2019 (n=68)
Jan–Mar 2020 (n=59)
Apr–Jun 2020 (n=56)
B
Patient interval
P25–Median–P75
p=0.011
p=0.008
PI (weeks)
0.6
1.0
2.7
1.1
C
System interval
P25–Median–P75
p=0.281
SI (weeks)
1.5
3.4
2.0
2.1


A
Total diagnostic interval
P25–Median–P75
p=0.128
TDI (days)
40
30
20
10
0
21
14
21
15
Jan–Mar 2019 (n=44)
Apr–Jul 2019 (n=54)
Jan–Mar 2020 (n=43)
Apr–Jul 2020 (n=46)
B
Patient interval
P25–Median–P75
p=0.041
PI (days)
21
14
21
14
C
System interval
P25–Median–P75
p=0.094
SI (days)
0
0
0
0

Version 1.1 2020-05-13

COVID Pandemic study of urgent clinical presentations of childhood malignancy and new cases of childhood diabetes to Children's Hospitals / Emergency Departments in UK: A Multicentre Quality Improvement project to inform public and professional guidance for children presenting with serious health concerns at the primary secondary care interface

Diabetes Mellitus

Centre:_____ **Gender**: ☐ Male ☐ Female

Age at diagnosis: ☐ Under 5 ☐ 5-11 ☐ 12 + **Patient from a BAME background:** ☐ Yes ☐No

- **Initial symptom(s)**

  ☐ polydipsia ☐ polyuria ☐ thirst ☐ lethargy ☐ weight loss
  ☐ other _____

- **Key dates (DD/MM/YYYY)**

  Date of first symptom onset: _____ ☐ Not known

  Date of first presentation to healthcare: _____ ☐ Not known

  Date of diagnosis: _____ ☐ Not known

  Date starting insulin treatment: _____ ☐ Not known

Establishing the exact date could be difficult. In this situation please approximate as described:
- *If the exact date can only be specified to the nearest week, please record this by entering the date of the first day of the week (Monday).*
- *If the exact date can only be specified to the nearest month, please record this by entering the first day of the month.*
- *If the information is not available, please select 'not known*

Route to diagnosis

- Was the patient in COVID-19 self-isolation/shielding?
  ☐ No
  ☐ Yes ☐ Confirmed case
  ☐ Possible contact with a confirmed case
  ☐ Clinical symptoms met
  ☐ Other _____

- Who was the first healthcare professional (HCP) they contacted about the symptom(s):
  ☐ GP ☐ Emergency doctor ☐ Paediatrician ☐Nurse practitioner ☐ Health visitor
  ☐ NHS 111 ☐ Other (please specify _____)

- How many HCP contacts before diagnosis? _____
- Patient's place of care when the definitive test (e.g. capillary/blood glucose) that identified the condition was requested:
  ☐ Primary care ☐ Outpatient ☐ Inpatient ☐ A&E ☐ Other _____

- Definitive test: ☐ Lab glucose ☐POCT glucose ☐ Other _____

  Result: _____

- Was this an incidental finding?

  ☐ No ☐ Yes - asymptomatic ☐ Yes - with non-specific symptoms

- What was the source of referral leading to diagnosis?

Emergency presentation (A&E)	☐ Self-referral ☐ GP referral ☐ MIU/Walk In Centre ☐ Emergency transfer from another hospital ☐ NHS 111 ☐ Other HCP (please specify) _____
GP referral	☐ Routine referral ☐ Urgent referral to general paediatrician ☐ Urgent referral to specialist diabetic services ☐ Other _____
Other	Please specify: _____

- Any other comments about the patient's journey to diagnosis

  _____

  _____

- Diabetic ketoacidosis at presentation

  ☐ No ☐ Yes

  Glucose level: _____
  pH at presentation: _____
  Ketones: _____
  Bicarbonate: _____
  GCS at presentation: _____
  Cerebral oedema: ☐ No ☐ Yes
  Fluid resuscitation: ☐ No ☐ Yes amount:_____
  Ventilation: ☐ No ☐ Yes _____ days
  ITU stay: ☐ No ☐ Yes _____ days

- **Antibodies:**

Islet cell cytoplasmic antibodies (ICA)	☐ Negative ☐ Positive	☐ Not tested
Glutamic acid decarboxylase antibodies (GAD)	☐ Negative ☐ Positive	☐ Not tested
Insulin autoantibodies (IAA)	☐ Negative ☐ Positive	☐ Not tested
Zinc Transporter 8 antibodies (ZnT8)	☐ Negative ☐ Positive	☐ Not tested
Insulinoma-associated-2 autoantibodies (IA-2)	☐ Negative ☐ Positive	☐ Not tested

Other: _____

Version 1.1 2020-05-13

COVID Pandemic study of urgent clinical presentations of childhood malignancy and new cases of childhood diabetes to Children's Hospitals / Emergency Departments in UK: A Multicentre Quality Improvement project to inform public and professional guidance for children presenting with serious health concerns at the primary secondary care interface

Paediatric Oncology

Centre: _____ **Gender**: ☐ Male ☐ Female

Date of admission: _____ **Age at diagnosis:** ☐ Under 5 ☐ 5-11 ☐ 12 +

Clinical Diagnosis: _____ **Patient from a BAME background:** ☐ Yes ☐No

At symptom onset

- **Initial symptom(s):**

  _____

  _____

- **Key dates (DD/MM/YYYY)**

  Date of first symptom onset: _____ ☐ Not known

  Date of first presentation to healthcare: _____ ☐ Not known

> ***Establishing the exact date could be difficult. In this situation please approximate as described below:***
> - *If the exact date can only be specified to the nearest week, please record this by entering the date of the first day of the week (Monday).*
> - *If the exact date can only be specified to the nearest month, please record this by entering the first day of the month.*
> - *If the exact date can only be specified to the nearest season, please record this by entering the first day of April for "spring", July for "summer" or "mid-year", October for "fall" or "autumn". In winter, attempt to determine whether the diagnosis was "late in the year" (use December with the applicable year) or "early in year" (use January with the respective year).*
> - *If the information is not available, please select 'not known*

Route to diagnosis

- Was the patient in COVID-19 self-isolation/shielding?

  ☐ No

  ☐ Yes ☐ Confirmed case
  ☐ Possible contact with a confirmed case
  ☐ Clinical symptoms met
  ☐ Other _____

- Who was the first healthcare professional (HCP) they contacted about these symptoms:

  ☐ GP ☐ Paediatric emergency doctor ☐ Paediatrician ☐ Dentist ☐ Pharmacist

  ☐ Optometrist ☐Nurse practitioner ☐ Health visitor ☐ School nurse

  ☐ NHS 111 ☐ Other (please specify _____)

- How many HCP contacts before diagnosis? _____ or ☐ 0-3 ☐ 4-6 ☐ 7-9 ☐10+

- Patient's place of care when the investigation that identified the tumour was requested:
  ☐ Primary care ☐ Outpatient ☐ Inpatient ☐ A&E ☐ Other _____

- Was this an incidental finding?
  ☐ No ☐ Yes - asymptomatic ☐ Yes - with non-specific symptoms

- What was the source of referral leading to diagnosis?

Emergency presentation (A&E)	☐ Self-referral ☐ GP referral ☐ Optician referral ☐ Dentist referral ☐ MIU/Walk In Centre ☐ Emergency transfer from another hospital ☐ NHS 111 ☐ Other HCP (please specify) _____
GP referral	☐ Two week wait ☐ Routine referral ☐ Urgent referral to general paediatrician ☐ Other _____
Other	☐ Active surveillance (please specify _____) ☐ Diagnosed by another specialty (e.g. ENT) ☐ Other _____

At the time of diagnosis

> ***Date of diagnosis:*** *the first date of diagnosis whether clinically or histologically established. Please record date of clinical diagnosis, date of imaging or date of biopsy, either from pathology report or MDT meeting.*

- Date of diagnosis: _____
  ☐ Clinical diagnosis ☐Blood test ☐Imaging ☐Biopsy/surgery ☐ Not known
  ☐ Other _____
- Did the patients need to be admitted to ICU to start treatment within 7 days of admission?
  ☐ No ☐ Yes

MDT

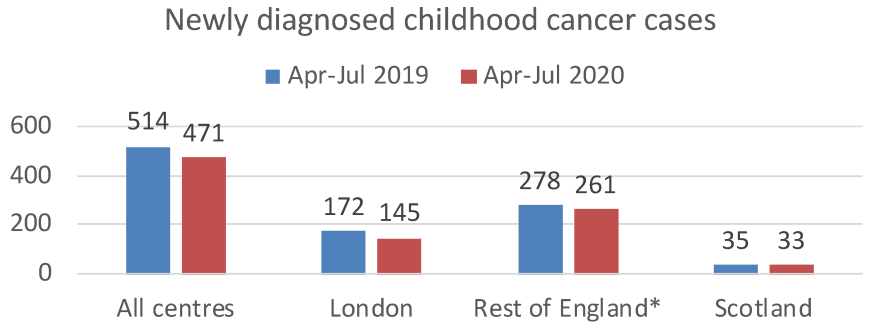
- Diagnosis (as agreed during MDT meeting): _____
- Tumour stage: _____
- Tumour size (as recorded in radiology report, largest dimension): _____
- Clinical risk group (if applicable): _____
- Date starting treatment: _____ ☐ Not known

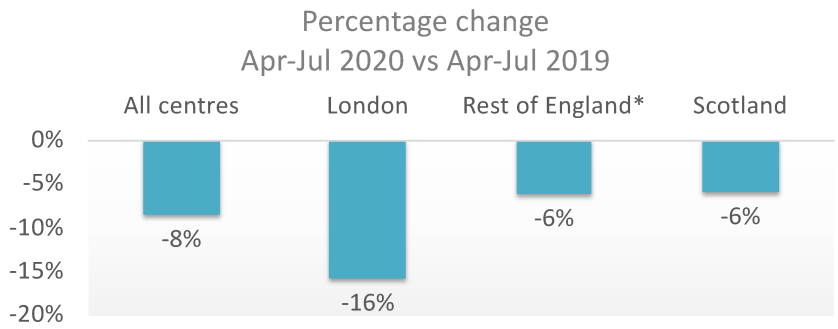
Incident childhood cancer cases during COVID-19 pandemic

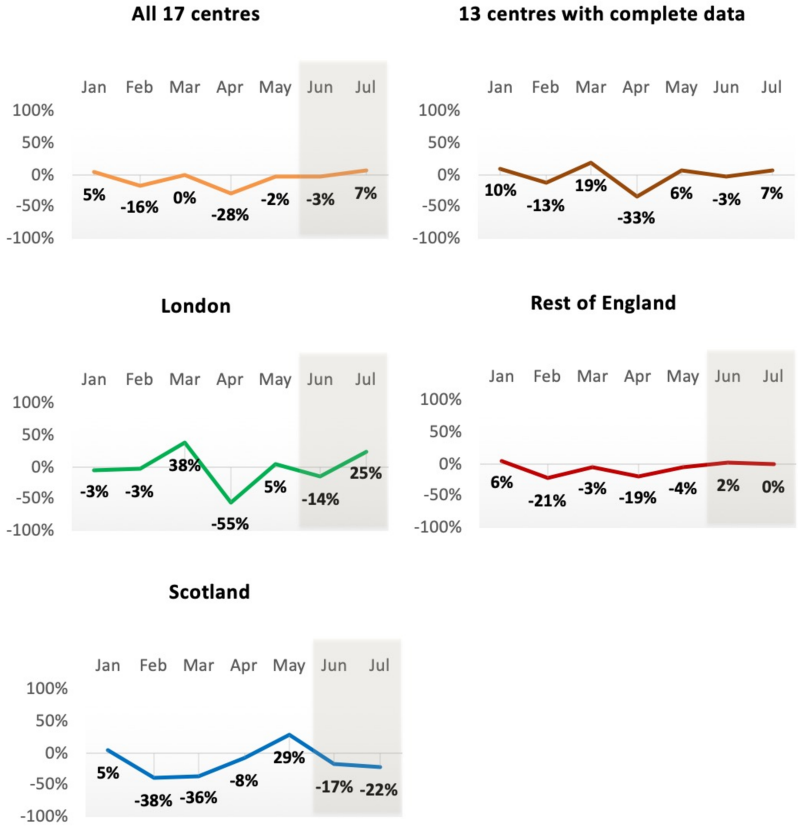
Jan-July 2020 vs Jan-July 2019

17 Centres, 2069 patients

Aberdeen, Belfast, Birmingham, Bristol, Cambridge, Cardiff, East Midlands, Edinburgh, Glasgow, GOSH, Leeds, Liverpool, Newcastle, RMH, Sheffield, Southampton, UCLH







Shaded area indicates incomplete data: No June and July data from Birmingham, Cardiff and Southampton